miR-19 is a key oncogenic component of mir-17-92.

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Public Summary:
Recent studies have revealed the importance of multiple microRNAs (miRNAs) in promoting cancer development, among which mir-17-92/Oncomir-1 exhibits potent oncogenic activity. Genomic amplification and elevated expression of mir-17-92 occur in several human B-cell lymphomas, and enforced mir-17-92 expression in mice cooperates with c-myc to promote the formation of B-cell lymphomas. Unlike classic protein-coding oncogenes, mir-17-92 has an unconventional gene structure, where one primary transcript yields six individual miRNAs. Here, we functionally dissected the individual components of mir-17-92 by assaying their tumorigenic potential in vivo. Using the Emu-myc model of mouse B-cell lymphoma, we identified miR-19 as the key oncogenic component of mir-17-92, both necessary and sufficient for promoting c-myc-induced lymphomagenesis by repressing apoptosis. The oncogenic activity of miR-19 is at least in part due to its repression of the tumor suppressor Pten. Consistently, miR-19 activates the Akt-mTOR (mammalian target of rapamycin) pathway, thereby functionally antagonizing Pten to promote cell survival. Our findings reveal the essential role of miR-19 in mediating the oncogenic activity of mir-17-92, and implicate the functional diversity of mir-17-92 components as the molecular basis for its pleiotropic effects during tumorigenesis.

Scientific Abstract:
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